Master of Science

Clinical outcome of hemodialysis access in liver transplanted patients

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Clinical outcome of hemodialysis access in liver transplanted patients

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All the honor and glory to the Lord.

But those who hope in the Lord
Will renew their strength.
They will soar on wings like eagles;
they will run and not grow weary,
they will walk and not be faint.
Isaiah 40:31

Clinical outcomes of hemodialysis access among liver transplant recipients

Abstract

Background End-stage renal disease (ESRD) is common following liver transplantation (LT). However, there is a scarcity of evidence to guide the selection of vascular access in LT patients who develop ESRD. This study aimed to compare the clinical outcomes of arteriovenous fistula (AVF) and arteriovenous graft (AVG) in LT and non-LT patients with ESRD.

Methods This study included 126 patients who underwent LT and required hemodialysis access creation between January 2006 and December 2021 (103 AVF and 23 AVG). The outcomes under study were rates of primary failure, complication rates, and primary and secondary patency among LT-ESRD patients. We compared outcomes of each LT-ESRD patient matched with two non-LT ESRD patients based on a basic characteristic score.

Results Out of 126 LT-ESRD patients, 103 (81%) received LT-AVF, and 23 (19%) received LT-AVG. The LT-AVG group had higher primary failure rates, as well as higher rates of thrombotic occlusion and infection, compared to the LT-AVF group ($p=0.003$, 0.001, and 0.032, respectively). Both primary and secondary patency rates were significantly higher in the LT-AVF group ($p=0.040$ and 0.009, respectively). No significant differences in clinical outcomes were observed between the LT and matched non-LT groups. Univariate and multivariate analyses indicated that AVG was associated with lower primary and secondary patency rates in all four groups (HR, 2.43; 95% CI, 1.61–3.68; $p<0.001$).

Conclusion In LT-ESRD patients, AVF demonstrated superior outcomes compared with AVG. There were no significant differences in the clinical outcomes of AVF and AVG between LT and non-LT patients. This study suggested the superiority of AVF over AVG in LT patients, mirroring findings in general ESRD patients.

Keywords: end-stage renal disease, liver transplantation, outcome, vascular access

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Introduction

Global organ transplantation rates have been consistently rising. In 2021, a total of 144,302 organ transplantations were performed, marking an 11.3% increase over 2020.[1] The liver is the second most commonly transplanted organ, accounting for 24% of all organ transplants.[1] The rate of liver transplantation (LT) also increased globally by 6.5% in 2021, constituting 34,694 cases—an increase of 20% from 2015.[2] This growth can be largely attributed to an increase in the number of deceased donors and the advancement of adult-to-adult living-donor LT. With the rising rate of LT, postoperative complications have also become more prevalent in clinical practice. Acute renal failure and chronic kidney disease are common complications following LT. The incidence of acute renal failure after LT ranges between 48% and 94%, with 8% to 17% of these patients requiring renal replacement therapy.[3]

The creation of a functional vascular access for hemodialysis (HD), maintaining its patency, and ensuring its adequacy are important factors directly impacting the survival of HD patients. According to the "fistula-first" strategy, an arteriovenous fistula (AVF) using a native vein as outflow should be considered the first option for every HD patient. However, the creation of vascular access for LT-end-stage renal disease (ESRD) patients is complicated due to the exhaustion of native veins caused by a prolonged course of chronic liver disease, which can necessitate multiple hospitalizations until its end stage and eventual transplantation. Furthermore, in the case of organ transplant recipients, the use of immunosuppressant drugs often dissuades the selection of a prosthetic vascular graft due to the common assumption that the insertion of a foreign body in immunosuppressed patients poses a high risk of graft infection.

The aims of this study were to describe the outcomes of AVF and arteriovenous graft (AVG) in LT-ESRD patients and to compare outcomes of each LT-ESRD patient matched with two non–LT-ESRD patients based on a basic characteristic score.

Methods

Study design and patient population

This retrospective observational study was conducted at Asan Medical Center in South Korea. It used data extracted from the medical records of LT-ESRD patients and non–LT-ESRD patients. The study protocol was approved by the hospital's institutional review board (IRB No. S2022-0525). Informed consent was waived due to the study's retrospective design, and all patient data were anonymized to protect privacy.

From January 1, 2006, to December 31, 2021, we identified patients who underwent LT and required HD access creation. We excluded patients whose HD access creation was not their first access surgery, those who underwent HD access creation before LT, those with insufficient medical records regarding access patency, those followed for less than 3 months after HD access creation, and those with maturation failure who never had access cannulation. A total of 126 patients were included, with 103 receiving AVFs (LT-AVF) and 23 receiving AVGs (LT-AVG).

We analyzed the clinical outcomes of access creation, including primary failure and complications, primary and secondary patency, and we examined associations between clinical variables and outcomes. To explore the impact of LT on HD access outcomes and patency, we matched the LT group with a non-LT group. For this purpose, we created a non-LT cohort by extracting medical records of patients who underwent HD access creation surgery between January 1, 2006, and December 31, 2021, and had no history of liver cirrhosis or LT. We excluded patients with missing information about HD access patency, those whose HD access operations were not their first, those followed for less than 3 months after HD access creation, and those using immunosuppressants within the previous 3 months.

We matched 1255 non–LT-AVF and 274 non–LT-AVG patients with the LT group at a 1:2 ratio based on basic characteristics. After stratifying and excluding patients with maturation failure and no cannulation from the non–LT-AVF (n=206) and non–LT-AVG (n=46) groups, we finalized groups of 193 non–LT-AVF patients and 46 non–LT-AVG patients. The same analyses were used to compare groups between LT-AVF and non–LT-AVF and LT-AVG and non–LT-AVG.

Definitions and study outcomes

Primary failure was defined as either a failure of maturation within 6 months of creation or the absence of cannulation. Early dialysis failure was defined as the inability to use an AVF for HD by the third month following its creation, despite radiologic or surgical interventions. Late dialysis failure was defined as the inability to use an AVF for HD by 6 months following its creation, despite radiologic or surgical interventions.

Primary patency was defined as the period from AVF creation to the first intervention due to thrombosis, stenosis, or other causes. Secondary patency was defined as the period from AVF creation to the permanent failure of AV access. The primary outcomes of our study were HD access primary and secondary patency, and the secondary outcome was HD access primary failure and clinical complications, including occlusion, stenosis, and infection.

Outcome definitions of HD access were determined according to the North American Vascular Access Consortium (NAVAC) criteria. Follow-up data were obtained from medical records, and the study outcomes were analyzed. All HD access creation procedures were performed under local anesthesia by specially trained vascular surgeons. PTFE graft materials were used in AVG creation. Patient risk factors of interest, clinical characteristics, and follow-up examination data were recorded in Excel (Microsoft Corp., Redmond, WA, USA).

Statistical analysis

Descriptive statistics were used to summarize patient characteristics. Categorical variables are reported as frequencies or percentages, and continuous variables are reported as means and standard deviations. The chi-square test or Fisher's exact test was used to analyze differences between the two groups for categorical variables, and t-tests or the Mann-Whitney U test were used for continuous variables.

Kaplan-Meier survival analysis was performed to analyze long-term event-free rates, and results were compared between groups using the log-rank test. Univariate and multivariate analyses of associations between clinical variables and primary and secondary patency were performed using Cox proportional hazards regression modeling. Variables included in the multivariable model were selected based on

statistical significance ($p<0.1$) from the univariable analysis, and hazard ratios (HRs) with 95% confidence intervals (CI) were determined. A p-value less than 0.05 was considered statistically significant. All statistical analyses were performed using SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA).

Results

LT-AVF vs LT-AVG

The study cohort consisted of 126 patients, 103 (81%) in the LT-AVF group and 23 (19%) in the LT-AVG group. The mean follow-up duration was 4.1±3.5 years. The baseline characteristics and clinical outcomes of the study sample are presented in **Table 1**. There were no significant intergroup differences in terms of demographic characteristics of risk factors, except that patients were older in the LT-AVG group ($p<0.001$), and malignancy was more prevalent in the LT-AVF group ($p=0.004$). The primary failure rate (<6 months) was higher in the LT-AVG group ($p=0.003$), and primary late failure (3-6 months) occurred more frequently in the LT-AVG group. Vascular access occlusion and infection events were more common in the LT-AVG group, with p-values of 0.001 and 0.032, respectively. There was a significant intergroup difference in the mean number of days that patients had to use permanent vascular catheters, respectively, for HD until the vascular access creation became fully functional. The mean number of catheter days was 105 in the LT-AVF group, compared with 49 days in the LT-AVG group ($p=0.001$).

Kaplan-Meier survival analysis revealed that primary and secondary patency were significantly longer in the LT-AVF group, with p-values of 0.04 and 0.009 (**Figure 1**), respectively. The primary patency rates at 1, 2, and 5 years were 90%, 87%, and 75%, respectively, in the LT-AVF group, compared with 78%, 65%, and 61% in the LT-AVG group. The secondary patency rates at 1, 2, and 5 years were 97%, 96%, and 93%, respectively, in the LT-AVF group, compared with 91%, 87%, and 78% in the LT-AVG group. Clinical variables associated with primary and secondary patency were analyzed using univariate and multivariate Cox proportional hazards regression analyses. In the adjusted models, multivariate Cox proportional hazard regression revealed that diabetes mellitus (DM) (HR, 2.59; 95% CI, 1.26-5.32; $p=0.009$)

was significantly associated with decreased primary patency (**Table 2**). Univariate Cox proportional hazard regression indicated that the type of vascular access (AVG; HR, 3.92; 95% CI, 1.31- 11.7; p=0.015) was significantly associated with decreased secondary patency (**Table 3**).

LT-AVG vs non–LT-AVG

The non–LT-AVG cohort was created by matching with the LT-AVG cohort at a 1:2 ratio, and differences in baseline characteristics were compensated through matching (**Supplemental Table 1**). There were no statistically significant differences in clinical complications between the groups (**Table 4**). Kaplan-Meier survival analysis revealed no differences between the groups regarding primary and secondary patency (**Figure 2**). The primary patency rates at 1, 2, and 5 years were 78%, 65%, and 61%, respectively, in the LT-AVG group, compared with 62%, 49%, and 49% in the non–LT-AVG group. The secondary patency rates at 1, 2, and 5 years were 91%, 87%, and 78%, respectively, in the LT-AVG group, compared with 84%, 73%, and 53% in the non–LT-AVG group.

LT-AVF vs non–LT-AVF

The non–LT-AVF cohort was created by matching with the LT-AVF cohort at a 1:2 ratio, and differences in baseline characteristics were compensated through matching (**Supplemental Table 2**). There were no statistically significant differences in clinical complications between the groups (**Table 5**). Kaplan-Meier survival analysis revealed no differences between the groups regarding primary and secondary patency (**Figure 3**). The primary patency rates at 1, 2, and 5 years were 90%, 87%, and 75%, respectively, in the LT-AVF group, compared with 81%, 75%, and 70% in the non–LT-AVF group. The secondary patency rates at 1, 2, and 5 years were 97%, 96%, and 93%, respectively, in the LT-AVF group, compared with 95%, 92%, and 88% in the non–LT-AVF group.

Variables associated with primary and secondary patency

We proceeded with an analysis of the association between clinical variables and primary and secondary patency in all four groups of patients using univariate and multivariate Cox proportional regression. Adjusted multivariate regression revealed that the type of vascular access (AVG) (HR, 2.43; 95% CI, 1.61-3.68; p<0.001) and age (HR, 1.02; 95% CI, 1.00- 1.03; p=0.035) were associated with significantly

decreased primary patency. Meanwhile, a higher body mass index (BMI, as a continuous variable) (HR, 0.93; 95% CI, 0.87- 0.98; p=0.011) was associated with increased primary patency (**Table 6**). In the same analysis, the type of vascular access (AVG) (HR, 4.72; 95% CI, 2.48- 8.96; p<0.001) was associated with significantly decreased secondary patency, while a higher BMI (as a continuous variable) (HR, 0.92; 95% CI, 0.85- 0.99; p=0.021) was also associated with increased secondary patency (**Table 7**).

Discussion

Existing literature on the outcomes of vascular access for HD reports that AVFs are associated with a significantly higher primary failure rate but also higher primary patency, primary-assisted patency, and secondary patency at 1, 2, and 5 years, compared with AVGs.[4-8] Our study aligns with these findings concerning primary and secondary patency, though we observed a higher primary failure rate associated with AVGs. Hajibandeh et al., in their recent systematic review and meta-analysis, reported a 32.3% primary failure rate in the AVF group, compared with 20.3% in the AVG group (p=.0005).[5] Conversely, our study showed a primary failure rate of 9% in the AVF group compared to 35% in the AVG group (p=0.003). This discrepancy could be attributed to the small size of the LT-AVG cohort in our study. Furthermore, the choice of AVG, despite the general avoidance of graft insertion in immunosuppressed patients due to increased infection risk, indicates poor vessel condition and potentially serious overall health in these patients.

LT recipients were matched with the non-LT cohort based on basic characteristics using a 1:2 ratio. Our findings revealed no significant differences in access patency and clinical complications between LT and non-LT cohorts in both the AVF and AVG groups. The infection rate of patients with AVGs in the LT cohort was comparable with that of the non-LT group, suggesting that the use of immunosuppressant drugs after LT does not increase infection rates associated with grafts. Therefore, access outcomes of LT patients do not differ significantly from those of non-LT end-stage renal disease (ESRD) patients.

Our findings for LT-AVF vs LT-AVG are generally consistent with the results of the meta-analysis of HD access by Hajibandeh et al., with the exception of the primary failure rate.[5] This suggests that creating

HD access for LT patients does not necessitate a protocol specific to LT patients; the existing guidelines would be sufficient and appropriate. Our multivariate analysis of the LT cohort identified DM and AVG as factors associated with decreased primary and secondary patency, respectively. Jeong et al. also reported decreased primary patency associated with older age and DM.[9]

In our multivariate analysis of all LT and non-LT participants, patient factors associated with decreased primary patency were AVG and older age, whereas a higher BMI was associated with increased primary patency. AVGs were associated with decreased secondary patency, while a higher BMI was associated with increased secondary patency.

Studies on BMI as a factor associated with vascular access patency have reported mixed results. Some studies have found obesity (BMI>29.5) to be a significant negative predictor of fistula maturation[10,11] and a correlate of higher rates of vascular access immaturation and reintervention.[12,13] In contrast, our study found a higher BMI to be a protective factor for primary and secondary patency. Unlike other studies, our study treated BMI as a continuous variable, not a categorical variable, which allowed us to deduce that if BMI increases by 1 unit, the HR of vascular patency increases proportionally. Additionally, our study had a lower mean BMI, fewer obese participants, and fewer overweight participants, which might explain the differing results from other studies.

Some literature suggests the short-term superiority of AVG. Thwaites et al. concluded, in their retrospective observational study, that the superiority of AVF in terms of access patency was especially evident beyond 18 months.[5] Allemang et al. also showed superior secondary patency up to 1.2 years associated with AVGs compared with AVFs, suggesting that for patients with limited life expectancy, AVGs may be an effective alternative to AVFs to reduce both catheter time and associated complications.[14] Patients with ESRD who have undergone LT and are on HD can be considered to have a limited life expectancy. The literature reports a 3.6-fold increase in mortality risk for these patients compared with kidney transplant recipients.[15] Bahirwani et al. determined a 35% mortality rate at a median of 1.6 years post-transplantation in LT-ESRD patients.[16]

Given that the benefits of AVFs) are realized over the long term: should an LT-ESRD patient with a shorter life expectancy benefit from an AVG with short-term superiority? This is a controversial issue, and this crucial question should always be considered when deciding on HD access for every LT ESRD patient. The decision should be tailored to each patient's specific circumstances.

Our study, however, showed a higher rate of primary failure associated with AVGs, suggesting that they may not be beneficial in the short term. Thwaites et al. also reported a significantly higher rate of AVG thrombosis, which becomes evident early in the life of the graft.[5] With regard to patients with limited life expectancy, a study on vascular access for older patients found that preemptive AVF placement is the best route to HD for older patients who can tolerate surgery and are expected to live more than 4 months.

Our study had several limitations, including its retrospective nature, small cohort size, and single-center design. We acknowledge potential selection and information biases may have affected our findings. The decisions about the type of HD access were mainly made by the surgeon based on vessel diameter, quality, and expectations regarding maturation failure. Finally, our study cohort consisted only of Korean Asians, and our findings may not be generalizable to other populations.

To our knowledge, our study was the first to investigate the clinical outcomes of HD access after LT. This study will aid vascular surgeons in making evidence-based decisions when creating HD access for LT patients.

Conclusion

In LT-ESRD patients, AVFs were found to be superior to AVGs in terms of primary failure, primary patency, secondary patency, and clinical complications (such as occlusion and infection). The clinical outcomes of LT-AVF patients did not differ from those of non–LT-AVF patients, and the same was observed when comparing LT-AVG with non–LT-AVG patients.

References

1. Norah A. Terrault, Claire Francoz, Marina Berenguer, Michael Charlton, and Julie Heimbach Liver Transplantation 2023: Status Report, Current and Future Challenges.

https://www.cghjournal.org/article/S1542-3565(23)00278-1/pdf

2. Global Observatory on Donation and Transplantation. Interna- tional reports on organ donation and transplantation activities 2021, 2022. Available at: www.transplant-observatory.org.

3. Rajesh YALAVARTHY, Charles L. EDELSTEIN, Isaac TEITELBAUM Acute renal failure and chronic kidney disease following liver transplantation. Hemodialysis international 2007; 11:S7-S12

4. Thwaites SE, Holt SG, Yii MK. Inferiority of arteriovenous grafts, in comparison to autogenous fistulas, is underestimated by standard survival measures alone. ANZ J Surg. 2021 Jan;91(1-2):162-167. doi: 10.1111/ans.16472. Epub 2020 Dec 8. PMID: 33295103.

5. Hajibandeh S, Burton H, Gleed P, Hajibandeh S, Wilmink T. Impact of arteriovenous fistulas versus arteriovenous grafts on vascular access performance in haemodialysis patients: A systematic review and meta-analysis. Vascular. 2022 Dec;30(6):1021-1033. doi: 10.1177/17085381211041473. Epub 2021 Aug 31. PMID: 34461784.

6. Arhuidese IJ, Cooper MA, Rizwan M, Nejim B, Malas MB. Vascular access for hemodialysis in the elderly. J Vasc Surg. 2019 Feb;69(2):517-525.e1. doi: 10.1016/j.jvs.2018.05.219. PMID: 30683199.

7.Arhuidese IJ, Orandi BJ, Nejim B, Malas M. Utilization, patency, and complications associated with vascular access for hemodialysis in the United States. J Vasc Surg. 2018 Oct;68(4):1166-1174. doi: 10.1016/j.jvs.2018.01.049. PMID: 30244924.

8. Almasri J, Alsawas M, Mainou M, Mustafa RA, Wang Z, Woo K, Cull DL, Murad MH. Outcomes of vascular access for hemodialysis: A systematic review and meta-analysis. J Vasc Surg. 2016 Jul;64(1):236-43. doi: 10.1016/j.jvs.2016.01.053. PMID: 27345510.

9. Jeong S, Kwon H, Chang JW, Kim MJ, Ganbold K, Han Y, Kwon TW, Cho YP. Patency rates of arteriovenous fistulas created before versus after hemodialysis initiation. PLoS One. 2019 Jan 28;14(1):e0211296. doi: 10.1371/journal.pone.0211296. PMID: 30689672; PMCID: PMC6349337.

10. Chan C, Ochoa CJ, Katz SG. Prognostic Factors for Arteriovenous Fistula Maturation. Ann Vasc Surg. 2018 May;49:273-276. doi: 10.1016/j.avsg.2018.01.069. Epub 2018 Mar 30. PMID: 29477678.

11. Arhuidese IJ, Holscher CM, Elemuo C, Parkerson GR, Johnson BL, Malas MB. Impact of Body Mass Index on Outcomes of Autogenous Fistulas for Hemodialysis Access. Ann Vasc Surg. 2020 Oct;68:192-200. doi: 10.1016/j.avsg.2020.04.009. Epub 2020 Apr 25. PMID: 32339695.

12. Raulli SJ, Sather K, Dicken QG, Farber A, Kalish JA, Eslami MH, Zhang Y, Cheng TW, Levin SR, Siracuse JJ. Higher body mass index is associated with reinterventions and lower maturation rates after upper extremity arteriovenous access creation. J Vasc Surg. 2021 Mar;73(3):1007-1015. doi: 10.1016/j.jvs.2020.04.510. Epub 2020 May 19. PMID: 32442609.

13. Alturkistani HM, Alsergani AH, Alasqah MI, Alsaif FF, Shukr MA. Predictors of recurrent arteriovenous fistula stenosis in Saudi patients undergoing hemodialysis. Saudi Med J. 2022 Jun;43(6):592-598. doi: 10.15537/smj.2022.43.6.20220192. PMID: 35675938; PMCID: PMC9389893.

14. Allemang MT, Schmotzer B, Wong VL, Lakin RO, Woodside KJ, Schulak JA, Wang J, Kashyap VS. Arteriovenous grafts have higher secondary patency in the short term compared with autologous fistulae. Am J Surg. 2014 Nov;208(5):800-805. doi: 10.1016/j.amjsurg.2014.01.010. Epub 2014 Apr 5. PMID: 24811929.

15. Eerhart MJ, Reyes JA, Leverson GE, Danobeitia JS, Blanton CL, Zitur LJ, Chlebeck PJ, Fernandez LA. Kidney After Liver Transplantation Matched-pair Analysis: Are Kidneys Allocated to Appropriate Patients to Maximize Their Survival? Transplantation. 2020 Apr;104(4):804-812. doi: 10.1097/TP.0000000000002870. PMID: 31335766; PMCID: PMC7313709.

16. Bahirwani R, Forde KA, Mu Y, Lin F, Reese P, Goldberg D, Abt P, Reddy KR, Levine M. End-stage renal disease after liver transplantation in patients with pre-transplant chronic kidney disease. Clin Transplant. 2014 Feb;28(2):205-10. doi: 10.1111/ctr.12298. Epub 2014 Jan 2. PMID: 24382253; PMCID: PMC3919458.

Table 1. Baseline characteristics and clinical outcomes of the study sample in LT patients

	AVF (n=103)	AVG (n=23)	p-value
Baseline characteristics			
Mean age. years	50.77 ± 7.76	57.96 ± 10.9	<0.001
Male sex	86 (83.5)	18 (78.3)	0.550
Body mass index, kg/m^2	22.17 ± 3.29	20.97 ± 3.12	0.114
Smoking			
Never	56 (54.4)	14 (60.9)	0.771
Ex-smoker	30 (29.1)	5 (21.7)	
Current	17 (16.5)	4 (17.4)	
Hypertension	77 (74.8)	14 (60.9)	0.179
Diabetes mellitus	74 (71.8)	15 (65.2)	0.528
Coronary artery disease	15 (14.6)	4 (17.4)	0.750
Cerebrovascular disease	12 (11.7)	5 (21.7)	0.196
Peripheral arterial occlusive disease	5 (4.9)	0 (0.0)	0.584
Chronic obstructive pulmonary disease	28 (27.2)	5 (21.7)	0.591
Malignancy	52 (50.5)	4 (17.4)	0.004
Hepatocellular carcinoma	44 (42.7)	3 (17.6)	0.051
Antiplatelet	49 (47.6)	13 (56.5)	0.438
Anticoagulant	13 (12.6)	3 (13.0)	>0.999
Statin	25 (24.3)	6 (26.1)	0.855
Clinical outcomes			
Primary failure (<6 months)	9 (8.7)	8 (34.8)	0.003
Early failure (<3 months)	4 (3.9)	3 (13.0)	0.114
Late failure (3-6 months)	5 (4.9)	5 (21.7)	0.018
Complications	32 (31.1)	12 (52.2)	0.055
Occlusion	5 (4.9)	7 (30.4)	0.001
Stenosis (>50%)	30 (29.1)	6 (26.1)	0.771
Infection	0 (0.0)	2 (8.7)	0.032

Continuous data are presented as means ± standard deviations; categorical data are given as n (%).

AVF, arteriovenous fistula; AVG, arteriovenous graft; LT, liver transplantation

Table 2. Univariate and multivariate Cox regression analyses of primary patency in LT patients

	Univariate		Multivariate	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Arteriovenous graft	1.96 (0.97, 3.96)	0.061	1.90 (0.94, 3.85)	0.073
Age	1.01 (0.98, 1.05)	0.431		
Female sex	0.92 (0.47, 2.00)	0.924		
Body mass index	0.94 (0.85, 1.03)	0.174		
Current smoking	0.61 (0.25, 1.47)	0.267		
Hypertension	0.63 (0.34, 1.15)	0.129		
Diabetes mellitus	2.63 (1.28, 5.39)	0.008	2.59 (1.26, 5.32)	0.009
CAD	1.63 (0.78, 3.37)	0.192		
CVD	1.56 (0.73, 3.35)	0.251		
PAOD	1.15 (0.35, 3.77)	0.814		
COPD	1.38 (0.75, 2.52)	0.299		
Malignancy	0.78 (0.44, 1.39)	0.400		
HCC	0.99 (0.54, 1.81)	0.967		
Antiplatelet	0.89 (0.50, 1.58)	0.695		
Anticoagulant	0.88 (0.35, 2.23)	0.792		
Statin	1.25 (0.68, 2.30)	0.483		

CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CVD, cerebrovascular disease; CI, confidence interval; HCC, hepatocellular carcinoma; HR, hazard ratio; LT, liver transplantation; PAOD, peripheral arterial occlusive disease

Table 3. Univariate Cox regression analysis of secondary patency in LT patients

	Univariate	
	HR (95% CI)	p-value
AVG	3.92 (1.31, 11.7)	0.015
Age	1.01 (0.95, 1.08)	0.670
Female sex	1.18 (0.33, 4.22)	0.805
Body mass index	1.00 (0.85, 1.18)	0.958
Current smoking	0.31 (0.04, 2.39)	0.259
Hypertension	0.44 (0.15, 1.27)	0.127
Diabetes mellitus	0.89 (0.29, 2.69)	0.834
CAD	2.05 (0.64, 6.6)	0.228
CVD	1.06 (0.24, 4.75)	0.939
PAOD	1.60 (0.27, 12.4)	0.651
COPD	0.99 (0.31, 3.16)	0.987
Malignancy	0.80 (0.28, 2.32)	0.685
HCC	0.99 (0.30, 3.31)	0.992
Antiplatelet	1.26 (0.44, 3.66)	0.669
Anticoagulant	0.54 (0.07, 4.13)	0.553
Statin	0.76 (0.21, 2.71)	0.666

CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CVD, cerebrovascular disease; CI, confidence interval; HCC, hepatocellular carcinoma; HR, hazard ratio; LT, liver transplantation; PAOD, peripheral arterial occlusive disease

Table 4. Clinical outcomes of AVG: LT vs non-LT patients

	AVG, LT (n=23)	AVG, Non-LT (n=46)	p-value
Primary failure (<6 months)	4 (17.4)	10 (24.4)	0.478
Early failure (<3 months)	1 (4.3)	7 (17.8)	0.247
Late failure (3-6 months)	3 (13.0)	3 (6.7)	0.406
Complications	12 (52.2)	31 (68.9)	0.176
Occlusion	7 (30.4)	22 (48.9)	0.145
Stenosis (>50%)	6 (26.1)	16 (35.6)	0.430
Infection	2 (8.7)	7 (15.6)	0.707

Categorical data are given as n (%).

AVG, arteriovenous graft; LT, liver transplantation

Table 5. Clinical outcomes of AVF: LT vs non-LT patients

	AVF, LT (n=103)	AVF, Non-LT (n=206)	p-value
Primary failure (<6 months)	9 (8.7)	26 (12.6)	0.310
Early failure (<3 months)	4 (3.9)	9 (4.4)	>0.999
Late failure (3-6 months)	5 (4.9)	3 (1.5)	0.122
Complications	32 (31.1)	60 (30.9)	0.980
Occlusion	5 (4.9)	26 (13.4)	0.022
Stenosis (>50%)	30 (29.1)	49 (25.3)	0.473
Infection	0 (0.0)	2 (1.0)	0.545

Categorical data are given as n (%).

AVF, arteriovenous fistula; LT, liver transplantation

Table 6. Univariate and multivariate Cox regression analyses of primary patency: LT and non-LT patients

	Univariate		Multivariate	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Arteriovenous graft	3.01 (2.08, 4.38)	<0.001	2.43 (1.61, 3.68)	<0.001
LT	0.93 (0.66, 1.32)	0.678		
Age	1.02 (1.00, 1.03)	0.012	1.02 (1.00, 1.03)	0.035
Female sex	1.25 (0.82, 1.89)	0.298		
Body mass index	0.93 (0.88, 0.98)	0.010	0.93 (0.87, 0.98)	0.011
Current smoking	1.11 (0.71, 1.73)	0.658		
Hypertension	0.97 (0.68, 1.39)	0.885		
Diabetes mellitus	0.97 (0.65, 1.45)	0.874		
CAD	1.40 (0.91, 2.16)	0.128		
PAOD	1.27 (0.65, 2.50)	0.489		
CVD	1.19 (0.74, 1.91)	0.481		
COPD	1.07 (0.74, 1.55)	0.721		
Malignancy	0.71 (0.50, 1.01)	0.056	0.86 (0.59, 1.25)	0.430
Antiplatelet	1.19 (0.85, 1.66)	0.312		
Anticoagulant	1.27 (0.79, 2.07)	0.327		
Statin	1.24 (0.86, 1.79)	0.243		

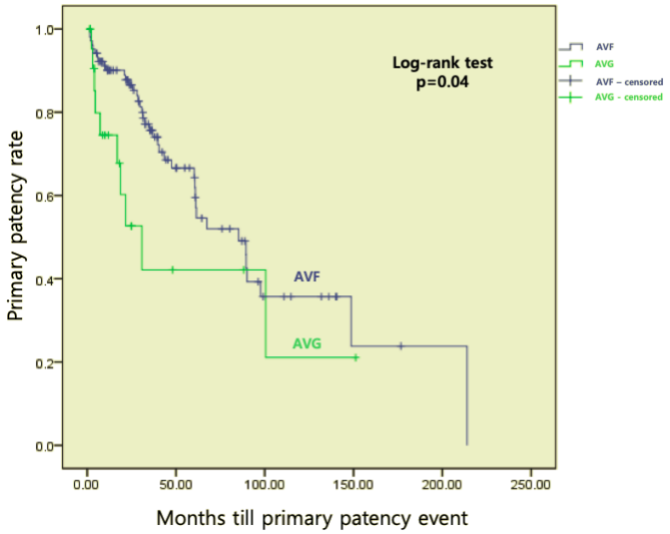
CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CVD, cerebrovascular disease; CI, confidence interval; HCC, hepatocellular carcinoma; HR, hazard ratio; LT, liver transplantation; PAOD, peripheral arterial occlusive disease

Table 7. Univariate and multivariate Cox regression analyses of secondary patency: LT and non-LT

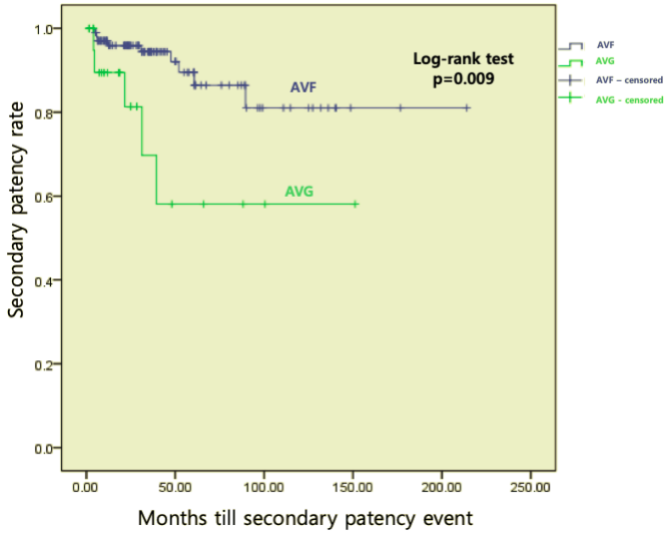
	Univariable		Multivariable	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Arteriovenous graft	6.24 (3.67, 10.6)	<0.001	4.72 (2.48, 8.96)	<0.001
LT	0.73 (0.40, 1.34)	0.312		
Age	1.02 (1.00, 1.04)	0.049	1.01 (0.99, 1.04)	0.312
Female sex	1.39 (0.75, 2.59)	0.299		
Body mass index	0.93 (0.88, 0.98)	0.010	0.92 (0.85, 0.99)	0.021
Current smoking	0.76 (0.36, 1.57)	0.756		
Hypertension	0.75 (0.43, 1.30)	0.300		
Diabetes mellitus	0.76 (0.41, 1.39)	0.373		
CAD	1.41 (0.73, 2.74)	0.306		
PAOD	0.27 (0.04, 1.95)	0.194		
CVD	0.96 (0.43, 2.11)	0.911		
COPD	0.93 (0.51, 1.69)	0.818		
Malignancy	0.48 (0.26, 0.86)	0.014	0.86 (0.44, 1.68)	0.655
Antiplatelet	1.62 (0.94, 2.78)	0.080	1.28 (0.74, 2.21)	0.384
Anticoagulant	1.24 (0.59, 2.63)	0.568		
Statin	1.00 (0.55, 1.81)	0.996		

CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CVD, cerebrovascular disease; CI, confidence interval; HCC, hepatocellular carcinoma; HR, hazard ratio; LT, liver transplantation; PAOD, peripheral arterial occlusive disease

Figure 1. Kaplan-Meier survival curves of (A) primary patency and (B) secondary patency: LT patients

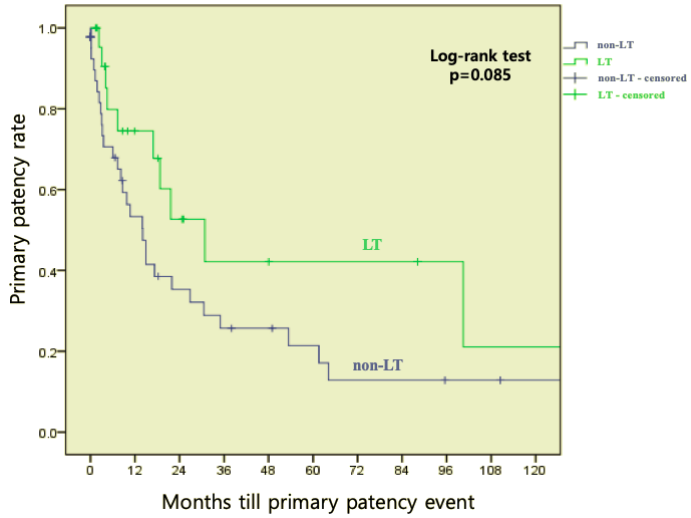


(A)

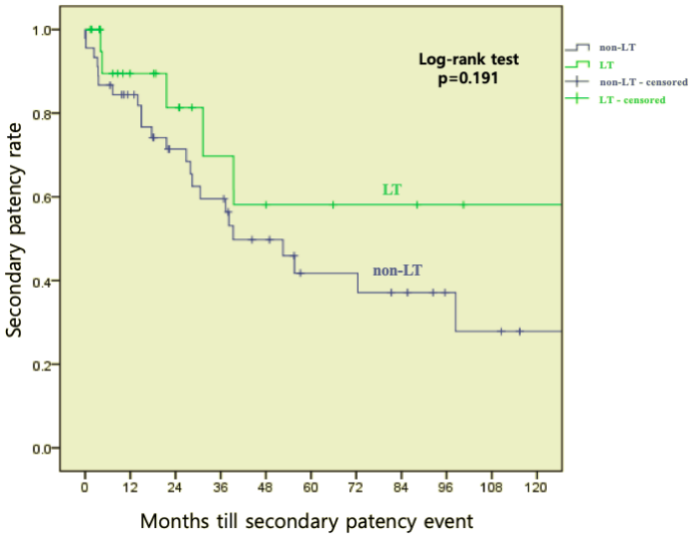


(B)

Figure 2. Kaplan-Meier survival curves of (A) primary patency and (B) secondary patency: LT vs non-LT patients (AVG)

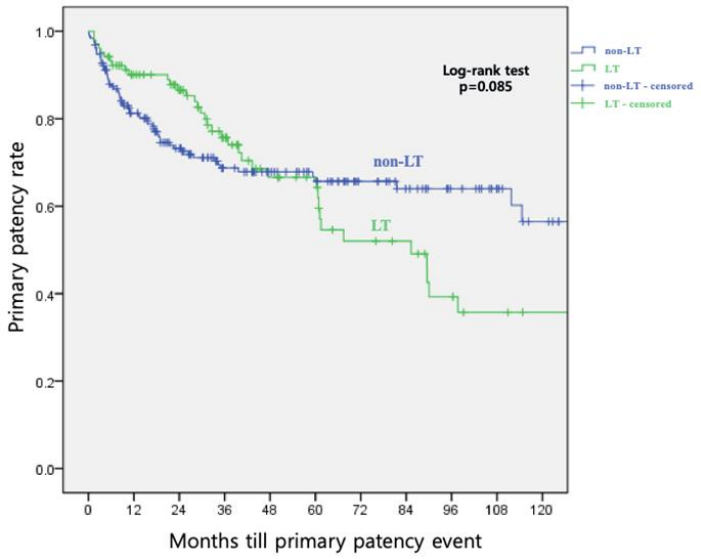


(A)

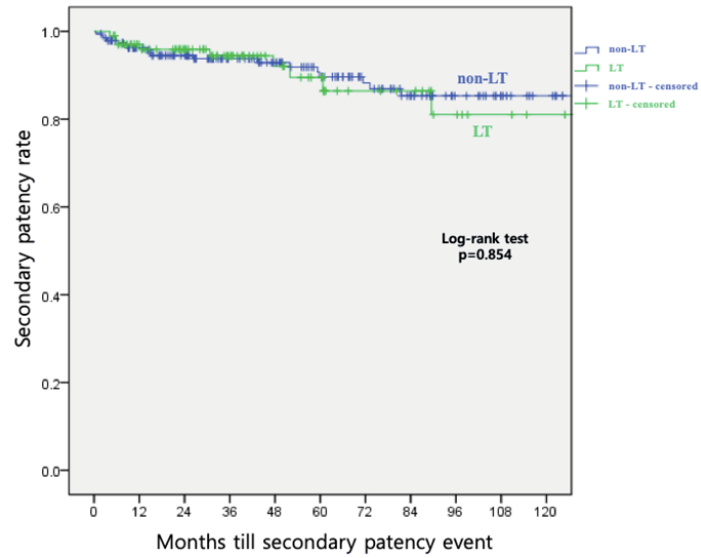


(B)

Figure 3. Kaplan-Meier survival curves of (A) primary patency and (B) secondary patency: LT vs non-LT patients (AVF)



(A)



(B)

Supplemental Table 1. Baseline characteristics of the study sample: LT vs non-LT patients (AVG)

		Unmatched			Matched (1:2)	
		AVG, LT (n=23)	AVG, non-LT (n=274)	p-value	AVG, non-LT (n=46)	p-value
Mean age. years		57.96 ± 10.9	66.58 ± 12.3	0.001	60.61 ± 14.1	0.433
Male sex		18 (78.3)	125 (45.6)	0.003	36 (78.3)	>0.999
Body mass index, kg/m^2		20.97 ± 3.1	23.34 ± 4.0	0.006	20.97 ± 3.8	0.995
Smoking	Never	14 (60.9)	204 (74.5)	0.295	30 (65.2)	0.817
	Ex-smoker	5 (21.7)	43 (15.7)		7 (15.2)	
	Current	4 (17.4)	27 (9.9)		9 (19.6)	
Hypertension		14 (60.9)	180 (65.7)	0.641	28 (66.7)	>0.999
Diabetes mellitus		15 (65.2)	257 (93.8)	<0.001	34 (73.9)	0.453
Coronary artery disease		4 (17.4)	103 (37.6)	0.053	6 (13.0)	0.441
Cerebrovascular disease		5 (21.7)	81 (29.6)	0.427	8 (17.4)	0.448
PAOD		0 (0.0)	32 (11.7)	0.151	0 (0.0)	
COPD		5 (21.7)	42 (15.3)	0.382	10 (21.7)	>0.999
Malignancy		4 (17.4)	70 (25.5)	0.385	8 (17.4)	>0.999
Antiplatelet		13 (56.5)	154 (56.2)	0.976	28 (60.9)	0.729
Anticoagulant		3 (13.0)	72 (26.3)	0.275	7 (15.2)	0.559
Statin		6 (26.1)	140 (51.1)	0.021	14 (30.4)	0.707

Continuous data are presented as means ± standard deviations; categorical data are given as n (%).

AVG, arteriovenous graft; COPD, chronic obstructive pulmonary disease; LT, liver transplantation; PAOD, peripheral arterial occlusive disease

Supplemental Table 2. Baseline characteristics of the study sample: LT vs non-LT patients (AVF)

		Unmatched			Matched (1:2)	
		AVF, LT (n=103)	AVF, non-LT (n=1255)	p-value	AVF, non-LT (n=206)	p-value
Mean age. years		50.77 ± 7.8	56.40 ± 13.5	<0.001	50.72 ± 15.0	0.975
Male sex		86 (83.5)	775 (61.8)	<0.001	165 (80.1)	0.471
Body mass index, kg/m^2		22.17 ± 3.3	23.66 ± 3.7	<0.001	22.49 ± 3.4	0.426
Smoking	Never	56 (54.4)	983 (78.3)	<0.001	109 (52.9)	0.762
	Ex-smoker	30 (29.1)	173 (13.8)		56 (27.2)	
	Current	17 (16.5)	99 (7.9)		41 (19.9)	
Hypertension		77 (74.8)	779 (62.1)	0.010	139 (67.5)	0.188
Diabetes mellitus		74 (71.8)	1164 (92.7)	<0.001	168 (81.6)	0.051
Coronary artery disease		15 (14.6)	352 (28.0)	0.003	29 (14.1)	0.908
Cerebrovascular disease		12 (11.7)	268 (21.4)	0.019	26 (12.6)	0.806
PAOD		5 (4.9)	97 (7.7)	0.287	13 (6.3)	0.606
COPD		28 (27.2)	208 (16.6)	0.006	54 (26.2)	0.855
Malignancy		52 (50.5)	260 (20.7)	<0.001	99 (48.1)	0.687
Antiplatelet		49 (47.6)	616 (49.1)	0.768	83 (40.3)	0.223
Anticoagulant		13 (12.6)	202 (16.1)	0.353	22 (10.7)	0.612
Statin		25 (24.3)	569 (45.3)	<0.001	55 (26.7)	0.646

Continuous data are presented as means ± standard deviations; categorical data are given as n (%).

AVF, arteriovenous fistula; COPD, chronic obstructive pulmonary disease; LT, liver transplantation; PAOD, peripheral arterial occlusive disease

초록

소개:

간 이식 환자에서 신부전이 합병증으로 동반되는 경우가 흔하며, 말기 신질환으로 이어질 시 혈액투석을 위한 적절한 혈관의 선택이 중요하다. 일반적으로 인조 혈관은 단기 및 중기 투석로의 개존율이 더 뛰어나지만, 자가혈관에 비해 감염 발생 위험이 더 높다. 본 연구는 간 이식 후 발생한 말기 신부전 환자에서 혈액투석을 위한 동정맥루의 임상적 결과를 분석하는 것을 목적으로 하였다. 또한 간 이식이 혈액 투석로 에 어떤 영향을 미치는지 알아보기 위해 혈액 투석을 받는 간 이식 환자와 일반 말기 신부전 환자의 혈액 투석로의 임상적 결과를 비교하였다.

통계방식:

본 연구는 단일 기관 후향적 관찰 연구로, 2006 년 1 월부터 2021 년 12 월까지 간이식 및 혈액투석 혈관 수술을 받은 126 명의 환자 (자가혈관 103 건 및 인조혈관 23 건) 를 포함하였다. 투석로의 임상적 결과는 일차실패율, 합병증 발생비율, 일차 및이차 개존율로 정의하였다.. 그리고 간이식 ESRD 환자 코호트를 비 간이식 ESRD 환자와 기본 특성 점수로 1 : 2 비율로 매칭하여 비교를 시행했다.

결과:

간 이식 ESRD 환자 코호트는 총 126 명으로, LT-AVF 103 명(81%) 및 LT-AVG 23 명(19%)이었다. 일차 실패율은 LT-AVG 그룹에서 더 높았다 (p=0.003). 투석 혈관 폐쇄 및 감염 사례는 LT-AVG 그룹에서 높았다(p=0.001, p=0.032). Kaplan-Meier 생존 분석에서는 LT-AVF 그룹에서 p-값이 0.04 와 0.009 로 일차 및 이차 개존율이 유의하게 더 높았다. Multivariate Cox 비례 위험 회귀 분석 결과 당뇨가 간 이식 ESRD 환자 투석로의 일차 개존율 감소와 유의한 관련이 있는 것으로 나타났다. (HR, 2.59; 95% CI, 1.26-5.32; p=0.009) LT 그룹과 비 LT 그룹의 매칭비교 분석에서는 투석 혈관의 임상

결과에 차이가 없는 것으로 나타났다. 4 개 그룹 모두에서일차 및 이차 개존율 분석과 임상 변수 연관성에 대한 단변량 및 다변량 Cox 비례 회귀분석에서 AVG (HR, 2.43; 95% CI, 1.61-3.68; p<0.001) 및 연령(HR, 1.02; 95 % CI, 1.00-1.03; p=0.035)은 일차 개존의 감소와 관련이 있는 한편, BMI(연속 변수)가 높을수록 (HR, 0.93; 95% CI, 0.87-0.98; p=0.011) 일차 개존의 증가와 관련이 있었다. 또한, 동일한 설정 분석에서 AVG (HR, 4.72; 95% CI, 2.48-8.96; p<0.001)가 이차 개존율의 감소와 유의한 관련이 있는 반면, 높은 BMI(HR, 0.92; 95% CI, 0.85-0.99; p=0.021) 가 이차 개존율 증가와 관련이 있었다.

결론:

LT-ESRD 환자의 혈액 투석 혈관 방식으로 AVF 는 AVG 에비해 일차 실패, 일차 개존율 및 이차 개존율 및 임상적 합병증 (폐쇄 및 감염) 측면에서 더 우월하였다. LT-AVF 대 non-LT-AVF 환자의 임상 결과는 유의한 차이가 없었으며, LT-AVG 대 non-LT-AVG 의 비교 결과도 마찬가지였다. BMI 가 높을수록 일차 및 이차 개존율이 증가한 반면 AV 는 짧은 1 차 및 2 차 개존율과 연관이있었다.